

101031, 607

Docket No. 2786-0199P

Please substitute the attached revised page 28 for the amended page 28 attached to the International Preliminary Examination Report.

IN THE CLAIMS:

Please cancel claims 1 through 25 without prejudice or disclaimer of the subject matter contained therein.

Please add the following claims:

--26. (New) An isolated nucleic acid sequence, of an alternative splicing variant of CD40 receptor (CD40R), selected from:

(i) the nucleic acid sequence depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 6; or

nucleic acid sequences having at least 90% identity with any one of the sequences of (i) over the entire length of the sequence.

27. (New) An isolated nucleic acid sequence complementary to the nucleic acid sequence of Claim 26.

28. (New) An amino acid sequence selected from the group consisting of:

(i) an amino acid sequence coded by the isolated nucleic acid sequence of Claim 26; and

Docket No. 2786-0199P

(ii) homologues of the amino acid sequences of (i) in which one or more amino acids has been added, deleted, replaced or chemically modified.

29. (New) An amino acid sequence according to Claim 28, as depicted in any one of SEQ ID NO:7 to SEQ ID NO;12.

30. (New) An isolated nucleic acid sequence coding with any one of the amino acid sequences of Claim 28.

31. (New) A purified antibody which binds specifically to an amino acid sequence present in any of the amino acid sequences of Claim 28 and not present in native CD40R.

32. (New) An expression vector comprising any one of the nucleic acid sequences of Claim 26 and control elements for the expression of the nucleic acid sequences in a suitable host.

33. (New) An expression vector comprising any one of the nucleic acid sequences of Claim 27, and control elements for the expression of the nucleic acid sequences in a suitable host.

34. (New) A host cell transfected by the expression vector of Claim 32.

Docket No. 2786-0199P

35. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of the expression vector of Claim 32.

36. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of any one of the amino acid sequences of Claim 28.

37. (New) A pharmaceutical composition according to Claim 35, for treatment of diseases which can be ameliorated, cured or prevented by decreasing the level of at least one ligand of CD40R.

38. (New) A pharmaceutical composition for treatment of diseases which can be ameliorated, cured or prevented by increasing the level of at least one of the CD40R variants of Claim 26.

39. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient any one of the nucleic acid sequences of Claim 27.

Docket No. 2786-0199P

40. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient the expression vector of Claim 33.

41. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier as an active ingredient the purified antibody of Claim 31.

42. (New) A pharmaceutical composition for treatment of diseases which can be ameliorated, cured or prevented by reducing the level of at least one of the CD40R variants of Claim 26.

43. (New) A method for detecting the presence of at least one variant nucleic acid sequence of CD40R in a biological sample, comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 26, and

(b) detecting said hybridization complex;
wherein the presence of said hybridization complex correlates with the presence of at least one variant nucleic acid sequence in the said biological sample.

44. (New) A method for determining the level of variant nucleic acid sequences of CD40R in a biological sample comprising the steps of:

Docket No. 2786-0199P

- (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 26; and
- (b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the at least one variant nucleic acid sequences in the sample.

45. (New) A method for determining the ratio between the level of the nucleic acid sequence of a CD40R variant in a first biological sample and the level of the original CD40R sequence from which the variant has been varied by alternative splicing, in a second biological sample comprising:

- (a) determining the level of the CD40R variant nucleic acid sequence in the first biological sample according to the method of Claim 44,
- (b) determining the level of the CD40R original sequence in the second biological sample; and
- (c) comparing the levels obtained in (a) and (b) to give said ratio.

46. (New) A method according to Claim 45, wherein said first and said second biological samples are the same sample.

47. (New) A method according to Claim 45, wherein the nucleic acid material of said biological sample are mRNA transcripts.

Docket No. 2786-0199P

48. (New) A method according to Claim 46, where the nucleic acid sequence is present in a nucleic acid chip.

49. (New) A method for identifying candidate compounds capable of binding to the amino acid sequence of Claim 28 and affecting the binding affinity of said sequences to at least one ligand of CD40, the method comprising:

- (i) providing any one of the amino acid sequences as defined in Claim 28;
- (ii) contacting a candidate compound with said amino acid sequence in the presence of at least one ligand of CD40;
- (iii) determining the effect of said candidate compound on the binding of said amino acid to said ligand and selecting those compounds which show a significant effect on said binding.

50. (New) A method for detecting any one of the amino acid sequences of Claim 28 in a biological sample, comprising:

- (a) contacting with said biological sample an antibody which binds specifically to an amino acid sequence present in any of the amino acid sequence of Claim 28 and not present in native CD40R, thereby forming any antibody-antigen complex; and

Docket No. 2786-0199P

(b) detecting said antibody-antigen complex wherein the presence of said antibody-antigen complex correlates with the presence of the desired amino acid in said biological sample.

51. (New) A method for detecting the level of any one of the amino acid sequences of Claim 28 in a biological sample, comprising:

(a) contacting with said biological sample an antibody which binds specifically to an amino acid sequence present in any of the amino acid sequences of Claim 28 and not present in native CD40R, thereby forming an antibody-antigen complex; and

(b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the level of said amino acid sequence in the sample.

52. (New) A method for determining the ratio between the level of any one of the amino acid sequences of Claim 28 of variant CD40R present in a first biological sample and the level of the original CD40R amino acid sequences from which they were varied by alternative splicing, present in a second biological sample, the method comprising:

(a) determining the level of the amino acid sequences of Claim 28 in a first sample;

Docket No. 2786-0199P

- (b) determining the level of the original CD40R amino acid sequence in the second sample; and
- (c) comparing the level obtained in (a) and (b) to give said ratio.

53. (New) A method according to Claim 52, wherein said first and said second biological samples are the same sample.